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PRINCIPAL INVESTIGATOR: Albert LoBuglio, M.D.
Mansoor Saleh, M.D.

CONTRACTING ORGANIZATION: The University of Alabama at Birmingham
Birmingham, Alabama 35294-0111

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6. AUTHOR(S)
Albert LoBuglio, M.D.
Mansoor Saleh, M.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

The University of Alabama at Birmingham
Birmingham, Alabama 35294-0111

E-Mail: Mansoor.Saleh@ccc.uab.edu

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This Clinical Trial Network was aimed at forming a collaborative linkage between the UAB Comprehensive Cancer Center, community-based oncology practices and pharmaceutical sponsors, and providing access to women with breast cancer within the community to high priority clinical trials. The dual review and oversight of all clinical trials conducted as part of this DOD funded Clinical Trial Network has exposed a number of differences in the interpretation of human subject protection standards between clinical trials conducted in the civilian academic setting and the DOD. As a result, activation of clinical trials has been slow at the onset given the lack of experience in dealing with DOD HSRB regulations and the interpretation of the DOD grant requirements. To-date one phase I/II clinical trial has been activated and two additional trials are in the final stages of the activation. Overall, the DOD funded Clinical Trial Network has the unique potential of providing access to women with breast cancer in the community to cutting-edge, novel therapeutic trials previously only available at academic centers. With the experience gained to-date activation of additional trials should proceed rapidly in years two and three.

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Introduction

We have initiated a Clinical Trials Network linking the UAB Comprehensive Cancer Center with community oncology groups for the conduct of early breast cancer clinical al trials using reagents developed by Cancer Center scientists, collaborators at the NCI and/or pharmaceutical partners. The Network encompasses 20 full service oncology practices in metropolitan Atlanta and additional sites in Alabama with clinical research coordination and leadership provided by the UAB Cancer Center. The network activity is governed by a central IRB (UAB IRB) with centralized administrative oversight for budget and contracting (UAB Grants and Contracts Office), and data management and data analysis provided centrally by the Cancer Center's Clinical Studies Unit (Biostatistics Shared Facility).

The specific aims of our proposal are to:

1. Establish and operate an efficient clinical trials network linking the UAB Comprehensive Cancer Center with community oncologists for the specific purpose of promoting the conduct of innovative early clinical trials in the field of breast cancer.

2. Coordinate a collaborative relationship with pharmaceutical/bioindustry partners such that new treatment strategies using novel reagents can be designed and efficiently tested in patients with breast cancer.

3. Provide a web-based automated patient screening and enrollment system to promote efficient breast cancer patient accrual throughout the network.

4. Provide an efficient clinical trial management team and biostatistical analysis unit to ensure optimal data management, analysis and reporting.

Body

This is the first annual report for the UAB Clinical Trial Network (UAB-CTN) established in collaboration between the UAB Comprehensive Cancer Center and community-based oncology practices in Alabama and Georgia. To date the affiliation between UAB and Georgia Cancer Specialist has been established and a number of clinical trials are in the process of being activated within the Network. Given the novelty of this endeavor and the various regulatory and administrative hurdles that have had to be overcome in coordinating clinical research between an academic comprehensive cancer center, community-based oncology practices, the DOD HSRB, and the pharmaceutical sponsors, we have focused on activating studies within the UAB-GCS Network before expanding to include network sites in Alabama.

The past 12 months have been dedicated to the development of the research infrastructure at the network sites, training of DOD dedicated research personnel as well as clinic personnel who will be providing oncologic care to protocol patients. In addition, the past

12 months have been an uphill learning curve for the PI and co-PI in that the interaction between the University and pharmaceutical sponsors, which has been ongoing and well refined, has had to deal with the specific administrative, regulatory and institutional review requirements mandated by the DOD HSRB as part of this funding mechanism. This additional layer of regulatory and administrative review and oversight often appear to be in conflict with the operation of clinical trials as conducted in the civilian system and/or requires multiple additional steps of approval prior to initiation of a clinical trial as part of the DOD funded Clinical Trials Network.

One clinical trial is currently approved and accruing patients in the network, two clinical trials await final DOD approval. While the activation of clinical trials and enrollment of women onto high priority breast cancer trials has been slow, the past 12 months have been a learning curve and have established the basis to hopefully improve the clinical trials mechanism intended by the grant and to address the primary objective of the clinical trial, namely availability of novel breast cancer clinical trials to women in the community.

Key Research Accomplishments

The UAB Clinical Trial Network includes three designated research clinics in Atlanta drawing patients from 20 GCS clinics, including one phase I/II site dedicated to the conduct of early clinical trials, and two sites involved in the conduct of phase II/III clinical trials.

Breast cancer trials conducted at the network sites are supported by one research RN and one data manager at each of the network sites, as well as a central research administrative team providing administrative and regulatory coordination at the network. A majority of the effort of this first year has been devoted to:

a. Reorganization of the network into a central clinical trial delivery unit (three centrally located clinical research sites with referral of patients from all of the other 17 clinic sites, as opposed to having clinical trials conducted at each of the 20 clinic sites).

b. Training and education of the entire network staff via formal sessions conducted at UAB, including training specific to the conduct of clinical trials, human subject protection issues, adherence to General Clinical Practice guidelines relevant to the conduct of clinical trials, and protocol mandated documentation and regulatory responsibilities.

c. Meeting with UAB IRB and DOD HSRB to discuss the structure of the network, the dual role of the UAB IRB and the DOD HSRB

d. Meeting with pharmaceutical sponsors and agreement to incorporate individual trials to be conducted via the DOD clinical trials network mechanism.

e. Submission of clinical trials for administrative and human subject review to DOD HSRB and UAB IRB in a complementary fashion in order to expedite approval and activation.

Reportable Outcomes

Clinical Trials Network Milestone Events

- Award Notification – **March 2000**
  - Training and in-servicing of Network personnel – **December 1999 and again June 2000 and June 2001**
  - Submission of first UAB IRB approved clinical trial for review and approval to the DOD HSRB – **May 2000**
  - Meeting with Pharmaceutical sponsors and informal agreement to incorporate individual trials to be conducted via the DOD supported infrastructure – **December 2000 and May 2001**
  - Meeting with DOD HSRB to formally present the CTN concept – **April 2001**
  - Meeting with UAB IRB for formal incorporation of DOD approved trials into the UAB sponsored CTN – **April 2001**
  - Formal approval of first UAB-CTN protocol – **April 2001**
  - Reorganization of Network clinical research sites – **April 2001**
  - Enrollment of first patient onto UAB-CTN – **May 2001**

- The first clinical trial to be submitted to the DOD HSRB as part of this grant was a phase I/II study of the drug immunoconjugate BR96-Dox for women with breast cancer. The clinical trial was already active at the UAB Comprehensive Cancer Center and one site at Georgia Cancer Specialists was participating in the trial. Activation of the study as part of the DOD funded UAB-CTN mechanism required a complete revision of the consent form, review and approval process and sign off by UAB, DOD, and the Sponsor. The activation of this study as part of the DOD funded UAB-CTN took 11 months. Please see below.

Approved and Pending Clinical Trials

- **UAB 9912 – A Phase I/II Study Using SGN-15 (cBR96-Doxorubicin Immunoconjugate) in Combination with TAXOTERE® for the Treatment of Metastatic Breast and Colorectal Carcinoma**
  - Submission to DOD – May 23, 2000
  - DOD Conditional approval – August 2000
  - Formal DOD HSRB approval – April 26, 2001

- **UAB 0009 – A Phase I Clinical and Pharmacokinetic Evaluation of Oral CI-1033 Given as a Single Dose Daily in Patients with Advanced Nonhematologic Malignancies**
  - Submission to DOD – January 19, 2001
  - DOD Conditional approval – April 11, 2001
  - Formal approval pending – July, 2001

- **UAB 0047 – A Multicenter Phase III, Randomized Trial Comparing Docetaxel in Combination With Doxorubicin and Cyclophosphamide (TAC) Versus Doxorubicin and Cyclophosphamide Followed by Docetaxel (AC→T) as Adjuvant Treatment of Operable Breast Cancer HER2NEU Negative Patients with Positive Axillary Lymph Nodes**
  - Submission to DOD – January 19, 2001
  - Conditional approval – April 11, 2001
  - Approval of DOD required consent form changes by sponsor (pending) – July, 2001

Conclusions

The UAB-CTN provides a unique setup for the conduct of early phase I/II as well as phase II/III breast cancer clinical trials in the community setting. The DOD supported infrastructure provides the personnel support for the rapid accrual of patients onto high priority breast cancer clinical trials at the community level. While community-based oncology practitioners have access to a majority of patients with breast cancer, access to cutting edge and early clinical trials is generally restricted to academic centers. The DOD supported infrastructure provides the framework to implement such clinical trials within the community setting. The funding of clinical research centers within the community provides the impetus for committed and motivated community-based clinicians to conduct clinical trials in the community setting in exchange for access to such trials via a linkage to an academic center. Part of the added value of this funding mechanism is the training of research personnel at the community level thus increasing the pool of personnel who can be involved in the conduct on clinical trials.

The biggest obstacle to accrual of patient onto such clinical trials is the two-tiered system of regulatory review and approval mandated by the granting body. It is apparent that the system identified by the DOD, which functions well for army sponsored clinical trials, creates a major hurdle for the approval and activation of clinical trials within the civilian setting. Conversion of a trial ongoing within the community setting (as part of UAB's ongoing relationship with community-based oncology practices) into a formal DOD supported clinical trial often takes months in order to comply with the DOD HSRB requirement as well as the host university IRB requirement. This aspect of the activation process has been the most time consuming and labor intensive operation and has in many ways detracted from the principal objective of this proposal.

However it is hoped that with experience on both sides (academic center and DOD), better understanding of the requirements on part of the DOD HSRB and the UAB IRB, as

well as the adequate training of research personnel within the network, the second funding year of this proposal will see increased activation and patient accrual onto early breast cancer clinical trials.

References

None.

Appendices

None.